PATENT COOPERATION TREATY

REC'D 14 APR 2005
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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2005/000020	06.01.2005	30.01.2004

International Patent Classification (IPC) or both national classification and IPC
A61K47/40, A61K31/439, A61P41/00, A61P39/00

Applicant
PFIZER PRODUCTS INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/IB2005/000020

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 10 (IA)

because:

☒ the said international application, or the said claims Nos. 10 (IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3 and 4
	No:	Claims	1, 2 and 5-10
Inventive step (IS)	Yes:	Claims	3 and 4
	No:	Claims	1, 2 and 5-10
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: BERNSTEIN P R ET AL: "Discovery of novel, orally active dual NK1/NK2 antagonists" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS 22 OCT 2001 UNITED KINGDOM, vol. 11, no. 20, 22 October 2001 (2001-10-22), pages 2769-2773, XP002322876 ISSN: 0960-894X

D2: NAKATE T ET AL: "Improvement of pulmonary absorption of cyclopeptide FK224 in rats by co-formulating with [beta]-cyclodextrin" EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS 2003 NETHERLANDS, vol. 55, no. 2, 2003, pages 147-154, XP002322877 ISSN: 0939-6411

D3: US-B1-6 642 233 (DUCOUX JEAN-PHILIPPE ET AL) 4 November 2003 (2003-11-04)

D4: WO 00/73304 A (PFIZER PRODUCTS INC; CASTALDI, MICHAEL, JAMES; QUALLICH, GEORGE, JOSEP) 7 December 2000 (2000-12-07)

If not mentioned otherwise, the relevant passages are those mentioned in the International Search Report.

Art 33(2) The present application does not meet the requirements of Article 33(2) PCT, since the subject-matter of claims 1, 2 and 5-10 is not new.

D1 discloses a pharmaceutical composition for injection comprising a NK-1 antagonist (ZD6021) and hydroxypropyl beta cyclodextrin. Therefore, the subject-matter of claims 1, 2 and 5-10 is not new in the light of D1.

D2 discloses a pharmaceutical composition for injection comprising a NK-1 antagonist (FK224) and beta cyclodextrin. Therefore, the subject-matter of claims 1, 5, 6 and 8-10 is not new in the light of D2.

D3 discloses a pharmaceutical composition for injection comprising a NK-1 antagonist and cyclodextrin. Therefore, the subject-matter of claims 1, 2, 5 and 8-10 is not new in the light of D3.

Art 33(3) The present application does not meet the requirements of Article 33(3) PCT, since the subject-matter of claims 1, 2 and 5-10 does not seem to involve an inventive step.
D1, which is considered to represent the most relevant state of the art, discloses the subject-matter of present claims 1, 2 and 5-10.
The problem to be solved by the present invention may therefore be regarded as how to provide an improved medicament comprising a NK-1 antagonist.
The present application suggests to solve the problem posed by providing a combination of a NK-1 antagonist and cyclodextrin.

Taking into account the teaching of the cited prior art the following reasoning applies:

With respect to the subject-matter of claims 1, 2 and 5-10 the applicant's attention is drawn to the fact that even if novelty could be established over the above-cited prior art it is at present not clear wherein an inventive step may reside.

With respect to present claims 3 and 4 it is noted that there is no hint in the prior art to overcome irratibility of the injection site associated with administration of a compound as described by present formula (I). The present application demonstrates that combination of such a compound with a cyclodextrin results in improved injection site tolerance.
Therefore, the solution proposed by claims 3 and 4 of the present application is considered to be inventive in the sense of Article 33(3) PCT.

Art 33(4) For the assessment of the present claim 10 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The subject-matter of claims 1-9 is considered to be industrially applicable in the sense of Art 33(4) PCT.